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The

WASHINGTON UNIVERSITY

MEDICAL ALUMNI

QUARTERLY



PUBLISHED IN THE INTEREST OF  
THE UNIVERSITY AND THE ALUMNI

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Present and Future Financial Position of the School of Medicine

Report on the Organization of the Clinic

Enzymatic Reactions in Carbohydrate Metabolism

New Officers Announced

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Vol. X

JULY, 1947

No. 4

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# The Washington University Medical Alumni Quarterly

Vol. X

July, 1947

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## Present and Future Financial Position of the School of Medicine

### FOREWORD

Since the Alumni Association sent out a questionnaire on the clinic, several requests for further details have been received in the Dean's Office. This and the following article, previously published in the Faculty Footnotes, are printed for the information of the Alumni.

Changing economic and social conditions in the United States and in the world are exerting a profound influence on medicine and medical education. So far as schools of medicine are concerned the influence is felt in two major fields—the educational program, and the fiscal policy.

At the level of university education, decisions should be based primarily on educational standards. However, the means to put the desired program into effect occupy a prominent position in the minds of the administrators. My purpose in making this report to the staff of the School of Medicine is to give everyone a frank statement of the past and present financial position of the school and to solicit cooperation in solving the problems of the future.

The budget of the School of Medicine for the present year (1946-47) is \$1,044,939. This is allocated as follows:

Professional Salaries .....	53.5%
Nonprofessional Salaries .....	19.8
Expense .....	13.2
Equipment .....	2.5
Miscellaneous (Overhead, Unassigned, etc.) .....	11.0

Income to meet these expenses is made up as follows:

Endowment (Medical School) .....	34%
Endowment (General) .....	9
Tuition .....	23
Professional Fees .....	12
Term Educational Grants .....	10
Deficit .....	12

It should be noted that we find it necessary to budget a deficit, equal to 12 percent of the total, to meet present needs.

The budget for next year is \$1,224,195. Most of the increase is for salaries and represents an increase in individual salaries, and not additions to the staff. The sources of income are substantially the same with slight increases in tuition and professional fees, and slight decreases in term educational grants and deficit from reserves.



Although the amount of income from endowment, tuition, and professional fees will vary from year to year, these may be looked upon as continuing sources. On the other hand, income from term educational grants and expenditure from reserves come to an end.

In the past 15 years, generous term educational grants have made possible strengthening and expansion of many activities of the school. These have been as follows:

1. Rockefeller Foundation for the establishment of a department of neuropsychiatry in 1938. \$50,000 a year in 1938, 1939, 1940, 1941, 1942, and 1943. \$45,000 in 1944. \$40,000 a year in 1945 and 1946. Total to date \$425,000.
2. Rockefeller Foundation for general support of the clinical departments. \$40,000 a year for 10 years beginning in 1938. Total to date \$360,000.
3. Rockefeller Foundation for establishment of a department of preventive medicine and public health in 1944. \$8,000 in 1944, 1945, and 1946. Total to date \$24,000.
4. Commonwealth Fund for establishment of a department of preventive medicine and public health in 1944. \$10,000 in 1944, \$10,000 in 1945, and \$8,000 in 1946. Total to date \$28,000.
5. W. K. Kellogg Foundation for postgraduate education in 1945. \$50,000 in 1945 and 1946. Total to date \$100,000. (In addition the W. K. Kellogg Foundation gave \$16,800 in 1946 for a course in hospital administration but it is expected that this will not have to be replaced at the termination of the grant.)

Thus, since 1937 this school has received for educational purposes (in contrast with research) about \$937,000 from three foundations. In the past six months three to five year renewals have been secured on four of the five, but the foundations will not continue these grants indefinitely. The outlook for the next six years, if renewals are not given, is shown in the following table.

	R.F. Neuropsych.	R.F. Clinical	R.F. Prev. Med.	C.F. Prev. Med.	Kellogg Postgrad.	Deficit From 1946-47
1946-47	\$40,000	\$40,000	\$ 8,000	\$8,000	\$50,000	\$ —
1947-48	35,000	40,000	10,000	6,000	50,000	5,000
1948-49	35,000	0	8,000	4,000	0	99,000
1949-50	30,000	0	6,000	0	0	110,000
1950-51	30,000	0	4,000	0	0	102,000
1951-52	20,000	0	2,000	0	0	124,000
1952-53	0	0	0	0	0	146,000

In other words, to hold just what we now have and make no additions, a renewal of the grants or their replacement by a new source of income amounting to \$146,000 a year must be found by 1952 and some before then. Capitalized at 4 percent this is \$3,650,000.



The rate of expenditure from present reserves is even more serious. On July 1, 1946 the School of Medicine had a general reserve fund of \$267,431.54 from surplus accumulated on the accelerated program during the war years. About \$60,000 will be used in 1946-47, leaving roughly \$207,000 on July 1, 1947. The budgeted deficit for 1947-48 is \$96,512. On the basis of present salary schedules and cost of supplies and equipment the deficit cannot be reduced much below that level without a cut in staff or a retrenchment in the educational and research program. By spending all reserve funds (Walker Fund and Board of Directors Fund), it will be possible to cover deficits for about 5 years or until 1952. At that time, merely to hold our present position a new source of income totaling at least \$100,000 a year must be found. Capitalized at 4 percent this is \$2,500,000.

Thus, to replace the present term educational grants and expenditures from reserves, the School of Medicine must by 1952 secure new income amounting to \$246,000 or gifts of \$6,150,000 additional endowment. This does not take into account any expansion of present departments or addition of other departments, which manifestly must be done if this school is to continue to occupy a preeminent position in American medical education.

It is impossible to estimate accurately what the requirements for expansion will be. Even if the present inflationary trend should slow or reverse, it seems likely from past trends that not less than another \$250,000 annually will be needed in 5 to 10 years for salary increases of the staff, scholarships, and new activities. Capitalized at 4 percent this is \$6,250,000.

A summary of the financial needs of the school 5 years from now—\$475,000 to \$500,000 a year in income or its equivalent in endowment—\$11,875,000 to \$12,500,000. Where is this to come from? The traditional sources are capital gifts and tuition. Let us examine these two.

There are many factors to be considered in evaluation whether or not new endowment can be secured. The capital and the interest rate for each year since 1925 are as follows:

<i>Year</i>	<i>Capital</i>	<i>Interest Rate</i>	<i>Year</i>	<i>Capital</i>	<i>Interest Rate</i>
1925-26	4,226,380	5	1936-37	6,908,940	4½
1926-27	4,226,380	5	1937-38	6,823,650	4
1927-28	4,876,380	5	1938-39	6,791,130	4
1928-29	6,134,280	5	1939-40	7,021,750	4
1929-30	7,064,280	5	1940-41	6,978,575	4
1930-31	6,777,380	5	1941-42	6,978,575	3½
1931-32	6,768,660	5	1942-43	6,978,575	3½
1932-33	6,768,660	5	1943-44	6,978,575	3½
1933-34	6,908,940	4½	1944-45	6,978,575	3½
1934-35	6,908,940	4½	1945-46	7,170,233	3¾
1935-36	6,908,940	4	1946-47	8,884,837	4

A rapid survey of these figures shows that the school started in 1925 with about four and a quarter million yielding 5 percent. Between 1927 and



1930 (well remembered as a boom period) the capital increased to about \$7,000,000. Here it remained for 15 consecutive years but with a progressive decrease in interest from 5 to 3½ percent; actually from about \$340,000 to \$245,000. Only in 1946 were there signs again of interest in this type of gift, when two anonymous gifts of \$800,000 and \$700,000 swelled the total to almost nine million.

This twenty year period had in it boom times, depression, and war, but it had little of the present high tax structure. Even if we could expect in the next 5 years endowment equal to one-quarter of the past 20 years, it would amount to only \$1,500,000, about 12 percent of what is needed. As a matter of fact the needs of the school for additional buildings (one for the medical sciences and a dormitory) exceed what may be secured in large gifts. Hence, we may conclude that little or nothing to meet the year to year expenses may be expected in the future from additional endowment.

Income from tuition is made up of two elements—number of students, and tuition charge per student. No increase in the size of our student body is possible without sacrifice of quality of instruction.

It is likely that the maximum has also been reached as regards the charge per student. In fact, the cost to students of a medical education is already so great that it must be increasingly subsidized by scholarships.

The history of the charge for tuition (exclusive of special fees) in Washington University School of Medicine is:

<i>Year</i>	<i>Tuition</i>	<i>Year</i>	<i>Tuition</i>
1921	200	1930 increased to	400
1923 increased to	300	1938 increased to	500
1926 increased to	325	1945 increased to	562.50
1928 increased to	350		

Comparable figures in other privately endowed schools for the year 1945-46 were:

Johns Hopkins .....	627	Bowman-Gray .....	510
Cornell .....	622	Yale .....	506
Harvard .....	600	Rochester .....	500
Chicago .....	555	Northwestern .....	500
Columbia .....	538	Vanderbilt .....	465
St. Louis .....	536	Duke .....	450
Western Reserve .....	529		

It is possible that an increase to \$600 would be justified. This would yield for 360 students a total of \$13,500. However, if there is any other way to raise this sum it should be used.

Expendable gifts have never made up any significant part of the budget of this school, never over two percent, and we have never made a systematic effort to establish a continuation fund.

Continuation funds are provided by alumni and other interested people. The school has 3,400 living alumni. The ties of alumni to schools of



medicine, in fact to all professional schools, are never as close as to undergraduate colleges. This fact, taken with the experience of colleges in solicitation of continuation funds would indicate that not more than \$15,000 may be expected even if a real campaign were started. Perhaps another \$15,000 in pledges could be secured in annual gifts, or a total of \$30,000. This conclusion is supported by the experience of the University in the immediate prewar years when about \$100,000 was pledged for all schools in a continuation program.

It does not appear that the tradition sources of income for an educational institution—capital endowment, tuition, and continuation gifts—can possibly provide for the needs of the School of Medicine in the future.

If all estimated capital gifts are diverted to an expansion of physical plant, there will not be much more than \$50,000 at the outside to be secured from tuition increase and annual gifts. Yet, \$475,000 to \$500,000 are needed. Hence, other than the traditional sources of income must be sought out and exploited.

There are two new sources of income for medical education which have been discussed in the past two years: subsidy from government; and participation in the operation of a clinic for private patients in which a part of the income would be set aside for undergraduate and postgraduate medical education and medical research.

The acceptance for an educational grant from the state or federal government, except under circumstances not now defined, would tend to destroy the essentially private character of our university. In a decade the program of medical education in this country would be molded into a single pattern. The establishment of a federal system of medical care would be only a short step after medical education was federalized.

It therefore appears that the only desirable, foreseeable, and tangible source of additional income for our school lies in participation in a private clinic. Without more funds the school will inevitably become an average school, something no staff member, student, alumnus, or St. Louisan wishes.

As the dean, and therefore the spokesman for the school, I ask for the cooperation of every member of the staff in meeting educational, medical, and financial problems of the next 5 years. Everyone, whether part time or full time, doctor of medicine or doctor of philosophy, physician or nurse or technician, student or alumnus, is interested in only one thing—to see that Washington University School of Medicine continues as an outstanding private school in an increasingly socialized and federalized society. It is my judgment that it can not do so unless an affiliated private clinic is established at once. The only problem in my mind is how the clinic may



be started without prejudice to the present staff in either educational opportunities or facilities for private hospital practice; a problem which is solvable and will be solved.

*Robert A. Moore*  
Dean

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## Report of the Organization of the Clinic

During the past three years there has been full consideration of all factors in the establishment of a clinic. Perforce, much of the discussion has been at the level of generalities. It is not possible in any human undertaking to define details until certain broad policies have been delineated. Unfortunately, there has been a great deal of confusion and misunderstanding largely because the details were not known. It is our privilege in this communication to outline the thinking of the committee appointed about a year ago to devise ways and means. This report on three topics—the position of the part-time staff member, adequate physical facilities, and the organization of the clinic is made at this time in order to acquaint you, not with accomplished facts, but with our reflections on how best to initiate and operate a clinic and to seek your suggestions.

### POSITION OF THE PART TIME STAFF MEMBER

The clinical staff of a school of medicine may be arranged on one of three bases.

1. Full time, in which all faculty members are on salary.
2. Part time, in which all clinical staff members engage in the private practice of medicine, and give part time to the school.
3. Combined full time and part time.

This school of medicine, since 1915, has been committed to the last—a combined full time and part time clinical staff. The executive faculty has in the last year reiterated this policy on at least three occasions. It is our opinion that the part time staff member makes a real contribution to education, research, and service. Repeatedly in the last few years able, promising young physicians have been appointed to the staff of school and hospital—two within the past month.

No part of any plan contemplates dropping present part time staff members or discontinuing new appointments when these men are able and willing to participate in the educational program. We are sure you agree with us that these qualifications are logical for the staff of a university and the affiliated hospitals.



There is no plan to regiment present part time staff members into a clinic. Every person will be free to join or not without jeopardizing his position. We are proud of you, we need you, and we hope that at least some of you will join the clinic. For those who wish to remain in private practice, there will be opportunities to teach, to care for private patients in the hospital, and to work in the research laboratories.

#### ADEQUATE PHYSICAL FACILITIES

In order to keep this promise—a continuing place for able part time staff—it is apparent to everyone that new physical facilities must be built. Today, there are not even enough beds and space for the present needs. Hence, plans must include three major items: new beds for the present staff, new beds for the needs of the clinic, and new space for the clinic.

The development of the clinic must be gradual, yet the construction of hospital and clinic space must be carried out in fairly large steps. It is not feasible to build less than 100 to 150 beds as a unit. The cost of building construction today is extremely high and any plans must, therefore, be arranged with good judgment for the future, and be based on taking advantage of every possible economy.

The eventual plant contemplated is a new hospital building for about 700 beds, mostly for private patients. Even if it were possible to finance this project, patients would not be available to fill all the rooms. Hence, we must start with something on a smaller scale. Our present plan is to add new space for about 225 beds and to rearrange present facilities to house another 35 to 50 beds—a total of 265 to 275 new beds.

The construction of new space for 225 beds will take advantage of the solid foundations of some present buildings. New stories can be added more cheaply than an entirely new building can be constructed; for example, steam lines are in and elevator shafts are available. Specifically, we are thinking of four more stories on the Rand-Johnson building and four more stories on the Mallinckrodt Institute of Radiology.

The addition to the Mallinckrodt Institute requires further explanation. The department of radiology is nearing the same point that the hospitals reached several years ago—no space for needed expansion. Even without a clinic it must be enlarged in the not far distant future. What is more logical than to enlarge it now, use the space for hospital beds until a new hospital can be constructed, and then return it to radiology for the work this department must do if our medical center grows, as it must and will.

The rearrangement to accommodate another 35 to 50 beds in present buildings is essentially the more efficient utilization of space for patients and allocation of less space for accessory services and storage.



The problem of providing space for the clinic offices is a difficult one. There is little space which can be converted to that use without compromising some other activity. We believe that the present doctors' offices or an equivalent space should be kept for the needs of the part-time staff. We do not believe that any space in the present clinic building should be diverted to other use, because this activity is a definite service to the community. Only later can the two clinics be combined as one. Hence, we have concluded that a new building of about at least 15,000 square feet of floor space should be constructed. Our plans contemplate erection of this building on Audubon Avenue. It is not anticipated that this small pilot clinic will need more than 35 hospital beds for clinic patients.

May we emphasize in summary, that our plans include complete provision for the immediate needs of the clinic and also 265 to 275 new hospital beds, which will also be available to the present staff.

As the plans mature and the needs increase, a large clinic building and a new hospital building of 700 beds can be constructed. The addition to the Mallinckrodt Institute will be returned to radiology, and the small clinic building will be converted to a dormitory or a continuation center, both of which are needed.

When these plans for new construction can be activated is indefinite, but we hope satisfactory financing of them can be arranged in the near future. We can only assure you now that the establishment of a clinic, construction of a clinic building, and construction of new hospital facilities will go forward as an integrated program; no one part of the program will proceed without the other so that there will be no dislocation of facilities and staff.

#### ORGANIZATION OF THE CLINIC

The organization of the clinic has been a particularly troublesome subject. Each physician has a little different idea of how a group should be integrated. We wish to present now our thinking about some of the problems in viewpoint, administration, and organization of the clinic.

*Type of Patients and Fees.* The clinic would carry on the tradition of medicine that the physician treats persons from all economic levels and charges them in accordance with their ability to pay—nothing for the really indigent, moderate fee for the great middle class, and a somewhat larger fee for the well-to-do. Thus, the clinic would have all types of patients and render the same service to everyone regardless of the financial return. A business office would set the fee for each patient within a range recommended by the associate medical board for the specific service rendered.

All charges to patients would be on a fee-for-service basis. It is not



anticipated that the clinic would provide medical care on a flat-fee basis, but it would accept patients insured by others.

*Administrative Control.* As with all other institutions in the medical center, there is a lay Board of Managers who provide final determination of policy and fiscal and social stability. Inasmuch as the clinic is integrated with the other institutions, it is proper for this Board to be made up of representatives from these institutions—two from the University, two from Barnes, two from Children's, one from Maternity, and one from McMillan. If other hospitals should be established approximate representation would be given.

*Professional Control.* As with all the hospitals, recommendations concerning appointments and professional conduct of the clinic would originate in a medical board. Such a medical board already exists and it is logical that its jurisdiction should be extended to the clinic. However, inasmuch as the clinic is an expansion in the practice of medicine, it is also proper that there be greater representation from practicing physicians, either from those now on the hospital staffs or from those to be on the clinic staff. The reorganized medical board would be composed of the heads of clinical departments and six staff members elected by the entire clinical staff. Nomination and election of the six members would be so arranged that at least one represented primarily the staff of the Barnes Hospital, one the Children's Hospital, one the Maternity Hospital, one the McMillan Hospital, and one the Clinic. The elected members would serve terms of three years and would not be eligible for reelection.

The rearrangement of administrative responsibilities for the clinic is essentially a transfer of final determination of broad policies for the clinic from the Boards of Directors of the Washington University and the hospitals to the Board of Managers of the Washington University Clinic, Inc. It has been said that this would result in giving a lay board control over the practice of medicine; something to be avoided at all costs. The answer to this is clear and direct. Since this school and the affiliated hospitals were organized the lay boards of directors have exercised as much authority over the practice of the staff as the Board of Managers of the Clinic would in the proposed clinic. There has been no interference in the past and there is no reason to expect it in the future. If this is regimentation then every physician in every hospital and in every medical school in the United States is already regimented.

In order that those who are primarily engaged in practice in the clinic may be organized to deal with the problems of day to day operation, an associate medical board will be organized. Members shall consist of those serving as senior attending physicians in each department, whether full



time or part time. This board would be responsible for professional conduct in the clinic within policies set by the joint medical board and the Board of Managers.

*Board on Professional Personnel.* One of the most important problems in the successful operation of the clinic will be the determination of the initial salary of each permanent member and when increases shall be given. Recommendations to the Clinic Board of Managers on this involve many factors and hence should be done by a group rather than by an individual. A board on professional personnel would be created for this purpose. It would be made up of two members of the Board of Managers designated by that Board, two members of the joint medical board elected by that board, and two members of the associate medical board elected by that board. Each member would serve for five years and would be eligible for reelection for a second term. The director and business manager of the clinic and the dean of the School of Medicine would serve ex-officio.

Inasmuch as professional salaries constitute a large part of the total budget, it may be desirable to have the joint board on professional personnel serve as a budget committee of the Board of Managers.

*Type of Medical Practice.* The clinic is established to render care primarily to ambulatory and hospitalized patients. An initial visit to the home will not be made, but if a patient has been under care by the clinic staff, and an emergency makes necessary a home call, it will be made by a staff member. The patient will as soon as possible be brought to the clinic or hospital for continued treatment. Hence, there will be no misunderstanding with the general practitioners of the community.

*Physician-Patient Relation.* In order to preserve the physician-patient relation which is traditional in medicine, special arrangements will be made.

A patient who comes to the clinic and asks for a doctor by name will be sent directly to that member of the staff.

A patient who comes to the clinic for care and does not have a choice of physician will first go to the admitting physician. Here a brief history and examination will reveal the major specialty to which he or she should be assigned.

In both instances, the physician who first looks after the patient will establish the physician-patient relation. All requests for referrals and consultations will then come from that member, not from an admitting officer.

*Staff.* The staff of the clinic would be composed of both full time and part time members. The relative numbers of each would vary from time to time and would depend on the demands for service and the availability of personnel. Young physicians would from time to time join the staff on a temporary basis. After from three to five years, the more able would be



added to the permanent staff. Thereafter this person would have the same security of position as those with indeterminate tenure in the University now have.

Compensation to both full time and part time staff would be in the form of an annual salary based on ability, experience, and service to the clinic. The salary would not be calculated as a certain percentage of the actual sum earned for the clinic by the individual, although this would be true for the total salaries.

*Organization of the Clinic Staff.* Departmentalization of the clinic would follow the pattern in force in the school and hospitals. At present this consists of departments of:

Internal Medicine	Pathology
Neuropsychiatry	Pediatrics
Obstetrics and Gynecology	Preventive Medicine
Ophthalmology	Radiology
Otolaryngology	Surgery

The head of the department would be chief of the service in the clinic as he now is in the hospitals and present clinic. One of the attending physicians on each service, on nomination of the chief, and endorsement of the joint medical board, would be appointed as a senior attending physician. Supervision of the professional care of patients would be the direct responsibility of the senior attending physicians, acting singly on their own service, and collectively as the associate medical board.

*Titles in the Clinic.* Since the clinic would be a separate organization, those working in it would be given a distinctive title in the same way that the hospitals now give separate titles. The titles for members of the staff of the clinic would be:

Physician-in-Chief  
 Senior Attending Physician  
 Attending Physician  
 Associate Attending Physician  
 Assistant Attending Physician  
 Fellow

In addition some physicians will be appointed as consultants.

*Research and Teaching by the Staff of the Clinic.* Every member of the clinic staff would be encouraged to do research either in the clinic or in the laboratory and to teach. However, in order that there may be a fair allocation of expense, no member of the clinic staff drawing his entire salary from the clinic would be permitted to spend more than twenty percent of his time on investigation and teaching. If it seemed desirable for someone to spend more time in research and teaching, then a proportionate fraction of his salary would be transferred to the budget of the School of Medicine.



*Allocation of Expense.* The present high cost of medical care must not be increased in the clinic by allocation of some income for medical education and research.

It is generally agreed that if a group of physicians use the same physical facilities and the same nurses, receptionists, technicians, etc., the saving in contrast with individual provision for these "costs of practice," is about 15 percent. It is this 15 percent which would be allocated to medical education and research, and the cost for medical service to the patient would not be increased over the present scale for equal value.

Statistics collected by the Department of Commerce and by Medical Economics show that regardless of the economic state of the country about 40 percent of the gross income of the physician represents the costs of medical practice—that is, charges which he pays for rent, salaries of receptionists, nurses, and technicians, and medical supplies and equipment. The "take home" pay of the physicians is thus about 60 percent of his gross income.

It is planned in the clinic to have the salary account, the sum set aside for annuities and insurance (about 5 percent of the gross), and the sum set aside for reserves to approximate this 60 percent. From a study of the financial statements of other clinics this is an entirely feasible arrangement.

We wish then to emphasize that the percentage of the gross income which will be paid to the physician in the form of salary, bonus, security, and reserves to guarantee his salary through economic fluctuations will not differ materially from that which he would derive from individual private practice.

*Professional Salaries.* A clinic cannot be successful unless it attracts to the staff able clinicians and this cannot be done unless salaries are paid which are within the range of the potentialities of the person in private practice.

At the economic level of 1946 a range from \$6,000 to \$25,000 seems necessary. The young man who has finished a residency and is thus 4 to 5 years out of school would begin at \$6,000. The chiefs of the services would receive the higher ranges of salary. Increases would be made on the basis of ability and service to the clinic.

In comparing these salaries with those in private practice it should be remembered that this is clear salary; the person has no expense of practicing, and security for his family and his old age are provided. Thus, they are really salaries of \$10,000 to \$40,000.

Because of economic fluctuations from year to year and in order to provide real security, it seems best to divide the compensation to profes-



sional staff into base salary and bonus based on income; 75 percent and 25 percent respectively of the total salaries mentioned in the preceding paragraph. We would thus avoid what happened at some clinics during the early thirties; so-called permanent staff were dropped. There would also be gained the important incentive that total salary in any one year is related to total income of the clinic for that year.

*Security of Staff.* Of equal importance with the scale of professional salaries is the security of the staff member for himself and for his family. The clinic would provide this in three forms.

1. *Security of position.* As pointed out in a previous section, staff members would be appointed on a permanent basis after a probationary period of 3 to 5 years. The permanent appointment would carry the same security as similar position in the University now does for professors and associate professors.
2. *Security for retirement.* For each full-time member of the permanent staff the clinic would purchase and pay the premiums for an annuity policy maturing at 65 to 68. The relation of the annuity will vary with the economic state of the country but it is the intent to work toward one which will yield one-half the average annual salary while employed by the clinic.
3. *Security for family.* For each full-time member of the permanent staff, the clinic will purchase and pay the premiums for a life insurance policy equal to at least one year's salary in favor of the nearest relative.

For those serving the clinic on a part time basis in excess of twenty percent of full time, the clinic will pay a proportionate share on annuity or life policies carried by the individual.

For those who are over 45 years old when they first become permanent members, the obligations of the clinic shall be limited to the premium rate as of 45 years.

*Allocation for Medical Education and Research.* That fraction of the gross income which would be allocated to medical education and research, 15 percent, would be used for the following activities.

1. Scholarships to medical students. When the GI Bill lapses the need for scholarships—so that medicine will not become a profession of rich men's sons—will be great. Many estimate it to be 40% of the total tuition charges, which in this school would mean \$80,000 a year.
2. Adequate salaries for full time staff in preclinical and clinical departments primarily engaged in teaching and research.
3. Additions to the staff at strategic points as, biophysics, industrial medicine, geriatrics, etc.



4. Research funds for all members of the staff, preclinical and clinical, full time and part time, which cannot be secured from outside sources.
5. Fellowships for young men and women who wish more training than is given in the usual residencies, both clinical and preclinical.
6. Hospitalization of patients for teaching and research, who could not otherwise afford it.
7. Opportunities for intellectual advancement such as travel to meetings and visits to other laboratories by members of the staff.

In every one of these categories we are now deficient. If all could be accomplished, the position of our school would be immeasurably stronger.

The exact handling of these general funds for research and education involves many legal problems as relate to taxation. However, the general plan may be outlined as follows. Each spring the dean of the school, and those heads of departments who wish educational grants, and individual staff members who wish research grants, would make application to the proper authority (probably some corporation established for this specific purpose). The applications would be processed and first referred to a medical advisory committee made up of six to ten members of the staff best qualified to pass on the merits of the requests. The lay board of the authority, on the basis of anticipated income, would then allocate the sum available that year to those projects which gave the most promise. The medical advisory board would include members from the senior staff of the clinic.

*Size of the Clinic.* In contrast with private clinics and groups, this clinic would be organized as an integral part of the medical center. There would, therefore, be a definite limitation on the size beyond which we would not go.

The exact final size must remain for the future to determine in terms of the needs of the school and the community. At the moment we do not visualize a clinic larger than that needed for our educational program and for the needs of the region of the country from which patients would be drawn. The clinic would, of course, care for both indigent and semi-indigent patients. A financial structure can be sound if from 10 to 15 percent of all patients receive free service and another 15 to 20 percent pay less than cost. It should be emphasized that the proposed clinic would not interrupt the present services of this medical center to the local population who cannot afford private medical care.

*Summary:* In summary, may we reiterate that what has been presented in this report is not a final action by any group. Rather it represents the thinking of the committee appointed a year ago to devise ways and means



to establish the clinic. May we once again emphasize the four important principles which we have tried to follow:

First, that the position of the part time men on the faculty of this Medical School and on the staffs of the hospitals will not be jeopardized.

Second, that additional new facilities will be constructed so that there will be adequate space for both full time and part time staff.

Third, that the basic relations between the staff and board which obtain in hospitals and universities throughout the country will be followed in the organization of the clinic.

Fourth, that the principles which are so characteristic of medical service in the United States—a definite physician-patient relation and a dedication to humanitarian service—will be continued.

*Forest P. Tralles, Chairman*

*Frank R. Bradley*

*Robert A. Moore*

Committee of the Board of Managers  
Washington University Clinics Inc.

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## Enzymatic Reactions in Carbohydrate Metabolism\*

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More than 18 years have elapsed since the writer had the privilege of presenting before the Harvey Society his analysis of the factors involved in carbohydrate metabolism. The large amount of new information that has come to light in the intervening years cannot be reviewed here. In general progress has been registered along two separate lines of investigation, those carried out on (more or less) intact animals and those carried out with isolated enzyme systems. In the former category, to mention only some of the more recent work, we find such important results as the recognition that the anterior pituitary (Houssay) and the adrenal cortex (Long) participate in the regulation of the blood sugar level, while work falling under the latter category has given us detailed knowledge of the intermediary reactions of carbohydrate metabolism. It will be the purpose of this presentation to examine how far these two lines of investigation can be integrated.

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\* Reprinted from THE HARVEY LECTURE SERIES, XLI, 1945-1946, pages 253-272.



## EXPERIMENTS ON INTACT ANIMALS

Carbohydrate metabolism in the intact animal may be represented by a number of over-all reactions; the most important of these are:

- (1) The reversible reaction, glycogen  $\rightleftharpoons$  lactic acid.
- (2) The reversible reaction, glycogen  $\rightleftharpoons$  glucose.
- (3) Oxidation of carbohydrate to  $\text{CO}_2$  and  $\text{H}_2\text{O}$ .
- (4)  $\text{HCOH} \rightleftharpoons \text{CH}_2$ ; interconversions, e. g., of carbohydrate carbon to fat carbon or of protein carbon to carbohydrate carbon. These are explored most successfully by means of isotopic carbon.

Simultaneous determination of all these factors on the same animal has led to a type of experiment which is referred to as carbohydrate balance. It may be of interest to examine briefly what information concerning carbohydrate metabolism can be obtained from such balances.

Table 1 summarizes some of these experiments. The animals were first fasted for 24 hours, providing the basal values for groups A and B, while the basal values for group C were those obtained on group B after 4 hours of glucose absorption.

TABLE 1  
*Changes in the Distribution of Glycogen in Rats*  
Values are expressed in mg. per 100 gm. rat

Experimental conditions	Glycogen in liver	Glycogen in rest of body	Carbo- hydrate oxidized	Blood sugar (per 100 cc.)	Number of animals
A. Fasted for 24 hours					
<i>Basal values</i> .....	7	136	....	92	16
Fasted 48 hrs. ....	+ 3	-25	....	+ 8	21
Insulin (3 hrs.) .....	- 2	-34	56	-12	4
Epinephrine (3 hrs.) .....	+36	-57	....	+18	6
Hypophysectomized (3 hrs.) .....	....	-16	60	-10	6
B After 4 hours of glucose absorption					
<i>Basal values</i> .....	7	136	....	92	16
Controls .....	+192	+263	465	+58	10
Insulin .....	+ 75	+393	550	-28	7
Epinephrine .....	+212	+136	357	+98	8
C. 3-hour post-absorptive period					
<i>Basal values</i> .....	220	432	....	158	13
Controls .....	- 49	-167	220	-45	4
Insulin .....	-141	-188	434	-89	4
Epinephrine .....	+ 26	-298	263	+16	5

From the changes in glycogen distribution observed after injection of epinephrine, in conjunction with other experimental evidence, it was deduced that muscle glycogen is converted to liver glycogen by way of blood



lactic acid. This interpretation is supported by recent experiments of Stetten and Klein (1) on the uptake of deuterium into liver glycogen from deuterium oxide administered to the animals. They found that the newly formed liver glycogen after glucose feeding contained 38, after lactate feeding 57 and after epinephrine injection 56 per cent of the deuterium content of the body fluids, as compared to a theoretical maximum of 66 per cent. Glycogen synthesis from 3-carbon fragments would be expected to result in much more exchange of stably bound hydrogen than synthesis from glucose directly. The fact that the liver glycogen after epinephrine injection had the same isotope content as after lactate feeding supports the idea of the lactic acid cycle.

Other deductions which may be made from the experiments in table 1 are the following. Beginning with group A, it may be seen that fasting is characterized by a rigid economy of the carbohydrate reserves; there is hardly any change in the glycogen content of rats between 24 and 48 hours of fasting. After hypophysectomy the animals are losing their carbohydrate reserves much more rapidly than the normal animals; in fact, they lose more carbohydrate during 3 hours of fasting than do normal animals in 24 hours of fasting. The hypophysectomized animals resemble in this respect normal fasting animals injected with insulin. The indications are that the anterior pituitary exerts a restraining influence on carbohydrate metabolism and that this as well as a diminished secretion of insulin, represent regulatory mechanisms which come into play during fasting.

Indications of such a regulatory mechanism can be seen when one compares the amount of carbohydrate oxidized during glucose absorption in group B and in the post-absorptive period in group C. As the fast continues, carbohydrate oxidation is restricted more and more until it reaches a minimum which does not exceed appreciably the new formation of carbohydrate from other sources and this allows the glycogen content of the tissues to remain constant.

Injection of insulin during glucose absorption causes an increased utilization of sugar in the peripheral tissues. Here insulin is merely superimposed upon the animals' own, presumably optimal insulin secretion. During the post-absorptive period, injection of insulin causes a marked disturbance of the normal regulatory mechanism. Liver glycogen disappears 3 times as rapidly as in the control animals, while muscle glycogen is not much affected. At the same time the restrictive influences on carbohydrate oxidation which are characteristic for the post-absorptive period are removed and the animals are now oxidizing sugar at the same rate as during glucose absorption. The interpretation given to these experiments is that insulin is favoring a reaction concerned with the utilization of blood sugar in the



tissues and that the liver is breaking down glycogen more rapidly in order to meet the increased demand for blood sugar.

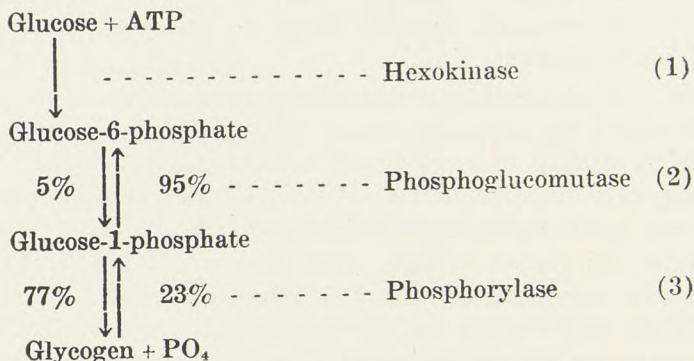
What reaction might be favored by insulin was not revealed by these experiments and after some consideration it was concluded that another approach was necessary in order to shed some light on this problem. Work on the whole animal was given up in favor of a study of individual enzymatic reactions. This involved the extraction of enzymes from the tissues and their separation from each other. In the course of this work several enzymes were crystallized, in particular phosphorylase (2), the enzyme which catalyzes the breakdown and synthesis of glycogen in the tissues.

#### EXPERIMENTS WITH ISOLATED ENZYME SYSTEMS

It was shown that the over-all reaction, glucose  $\longrightarrow$  glycogen, which is characteristic for the whole animal may be resolved into the following enzymatic steps (3).

The first reaction, catalyzed by hexokinase, an enzyme originally discovered by Meyerhof in yeast, and now known to occur in all animal tissues, is largely irreversible. In this reaction ATP (adenosinetriphosphate) is expended and this raises the problem of the regeneration of ATP.

The equilibria for the second and third reaction at pH 7, as determined for each enzyme acting separately, are shown above. Although the position of the equilibrium of the second reaction appears to be unfavorable, the over-all reaction will nevertheless proceed in the direction of glycogen synthesis as long as inorganic phosphate is being removed as fast as it is formed in the phosphorylase reaction. In the test tube this can be accomplished by the addition of barium ions which decrease the solubility of phosphate; in the intact animal the removal of inorganic phosphate is accomplished by



oxidation of carbohydrate which is coupled with the regeneration of ATP and thus permits ATP to be used again in the hexokinase reaction.



The over-all reaction, glycogen  $\rightleftharpoons$  lactic acid, has also been resolved into individual enzymatic steps, and these are embodied in the well-known Embden-Meyerhof scheme. Wood and collaborators (4) have found that glucose isolated from liver glycogen was labelled with heavy carbon in positions 3 and 4, when they administered glucose and  $\text{NaHC}^{13}\text{O}_3$  to fasting rats; labelling of these positions would be predicted from a reversal of the reactions of the Embden-Meyerhof scheme, following the incorporation of labelled carbon in the reaction, pyruvate +  $\text{CO}_2 \rightleftharpoons$  oxaloacetate.

One of the important results emerging from this work is the realization that carbohydrate oxidation is an offspring of the chain of reactions which lead from glycogen or from glucose to lactic acid. It is now generally agreed that carbohydrate oxidation at the pyruvate level is initiated by a condensation reaction between a  $\text{C}_2$  and  $\text{C}_4$  carbon compound; one oxidative cycle,  $(\text{C}_2 + \text{C}_4) \longrightarrow 2\text{CO}_2 + 2\text{H}_2\text{O} + \text{C}_4$ , regenerates the  $\text{C}_4$  compound (oxaloacetate) which can then again react with the  $\text{C}_2$  fragment derived from pyruvic acid. Here again experiments with carbon isotopes have given strong support to the general validity of a scheme of carbohydrate oxidation proposed by Krebs, although minor modifications of the original scheme appear necessary. The primary condensation product between  $\text{C}_2$  and  $\text{C}_4$  has not been identified, but assuming it to be a member of the tricarboxylic acid group, all further oxidative steps are known.

A greatly simplified scheme of carbohydrate metabolism, leaving out many of the intermediate steps, may now be presented (figure 1). The

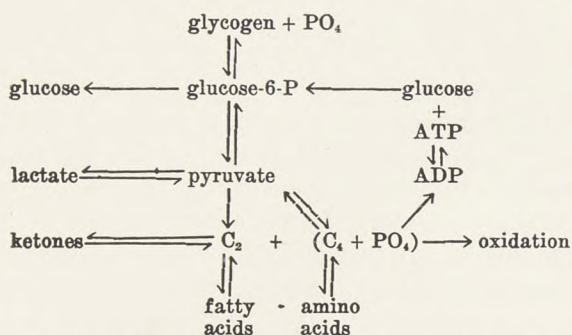


FIG. 1. Simplified scheme of carbohydrate metabolism.

main feature of this scheme, as far as this discussion is concerned, is that glucose in order to be metabolized must first react with ATP. Once glucose is converted to glucose-6-phosphate by the hexokinase reaction, several metabolic pathways are open. Glucose may become glycogen, it may be converted to fat, or it may be oxidized, and the magnitude of each transformation will depend on enzymatic equilibria determined by the metabolic



state of the animal. In a previously fasted rat about 50 per cent of the absorbed glucose is deposited as glycogen in liver and muscle, while the rest is oxidized (table 1), but once the glycogen stores are replenished, a large part of the absorbed glucose may be deposited as fat.

Blood sugar formation in the liver is due to the action of a specific phosphatase which converts glucose-6-phosphate to glucose and inorganic phosphate. In muscle such a phosphatase is absent and owing to this fact muscle contributes lactate instead of glucose to the blood stream. In both liver and muscle the concentration of inorganic phosphate within the cells should have a decisive influence on whether the reactions will proceed in the direction of glycogen synthesis or glycogen breakdown.

Similar effects of the concentration of other reacting substances exist. For example, the fate of the reactive 2-carbon fragments formed from fatty acids in the liver depends on the availability of  $C_4$  dicarboxylic acid (Lehninger (5)) ; in their absence the fragments condense with each other to form acetoacetate, in their presence the  $C_2$  intermediate is oxidized.<sup>1</sup> This oxidation and the regeneration of ATP (6).

It seemed likely that the regulation of the blood sugar level depends on special tissue structures sensitive to changes in the blood sugar concentration and on the release of hormones which would act on one or more of the enzymatic reactions discussed above. One example may be cited here, namely, the secretion of insulin by the islet tissue of the pancreas which is known to respond to the blood sugar level. The action of insulin in the intact animal has been investigated extensively, and since most of the intermediary reactions of carbohydrate metabolism are known, one would think that the mechanism of action of insulin would be amenable to investigation.

Krebs and Eggleston (7) have shown that the addition of insulin to minced pigeon breast muscle could under certain conditions prolong the oxygen consumption of these preparations. Their results have been confirmed by several investigators. In an over-all reaction of this type, composed of a large number of enzymatic steps which cannot be separated from each other, there would be considerable difficulty in finding out at what point, as shown in the scheme, is coupled with the uptake of inorganic phosphate in the chain of reactions insulin was exerting its effect. At least, this was the conclusion reached with respect to some observations made by Colowick and Sutherland in our laboratory in 1942 on cat liver dispersions.

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<sup>1</sup> Since the liver is the main site of formation of ketone bodies, it should be pointed out that the antiketogenic mechanism in the liver depends upon three reactions which lead to the formation of dicarboxylic acid, namely, pyruvate +  $CO_2 \rightleftharpoons$  oxaloacetate, transamination between pyruvate and either glutamate or aspartate, and direct deamination of these two amino acids.



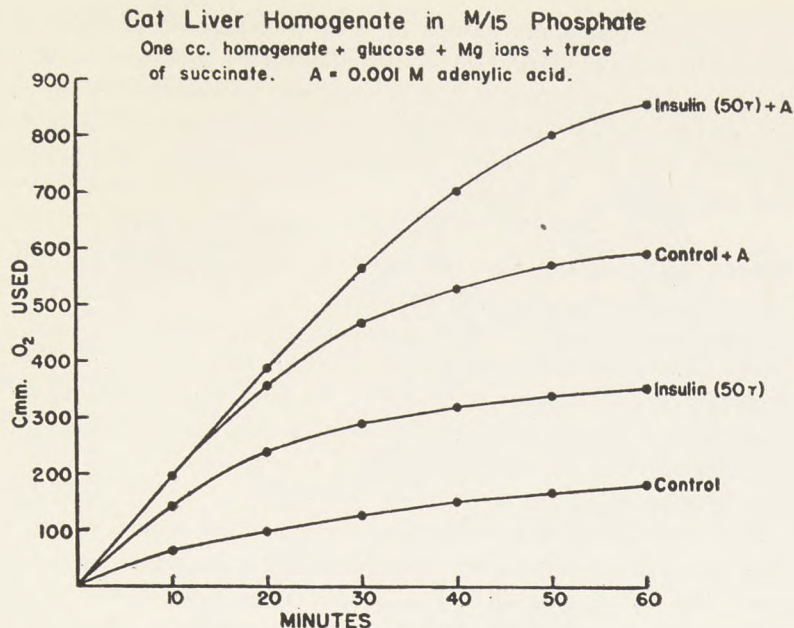


FIG. 2.

In contrast to the system investigated by Krebs, the rate of oxygen consumption was increased from the start when insulin was added. One of several rather striking experiments is shown in figure 2. The dialyzed homogenates were deficient with respect to adenine nucleotides, as shown by the effect of addition of adenylic acid. Without and with added adenylic acid insulin produced a very marked effect on the  $O_2$  consumption. The experiments have not been published so far, because in spite of much effort it has not been possible to control the system sufficiently to make the insulin effect regularly reproducible on different liver preparations, in itself an indication that the mechanism of action of insulin in this system is not understood.

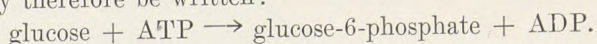
From time to time, when individual enzymatic reactions were being investigated, the effect of addition of insulin was tried, but a clear-cut effect on an isolated enzyme system *in vitro* could not be demonstrated. Although this led to the suggestion that the action of insulin and other hormones may depend on a more or less intact cell structure, the search for an *in vitro* effect of insulin was continued.

#### YEAST AND ANIMAL HEXOKINASE

A number of circumstances permitted us to investigate the hexokinase reaction. Colowick and Kalckar (8) had shown with hexokinase prepared from baker's yeast that this enzyme catalyzed a one-step reaction; only one



of the two labile phosphate groups of ATP (adenosinetriphosphate) was transferred to glucose. ADP (adenosinediphosphate) could not act as phosphate donor. They also showed that glucose was phosphorylated on carbon atom 6, giving rise to the formation of glucose-6-phosphate. Both points have recently been shown to apply also to brain hexokinase. The hexokinase reaction may therefore be written:



Colowick and Kalckar also developed a manometric method for the determination of hexokinase activity which is based on the fact that one acid equivalent is formed for each phosphate group transferred from ATP to glucose. Enzyme activity can also be followed chemically by determining the disappearance of glucose or of ATP. In most experiments to be discussed later the reaction was followed manometrically and a terminal glucose analysis was made on the contents of the Warburg vessels.

Yeast hexokinase has been prepared in crystalline form. This enzyme needs  $\text{Mg}^{++}$  for its activity as does the corresponding animal enzyme, but no other co-factor is needed. The animal hexokinase has so far been purified only partially. Hexokinase activity has been demonstrated in our laboratory in extracts of liver, kidney, brain, skin, intestine, anterior pituitary, heart and skeletal muscle. In the case of muscle and other tissues the hexokinase activity found was of sufficient magnitude to account for the rate of metabolism of glucose observed in these tissues in the intact animal.

Colowick and Price (9) have carried out a detailed study of rat muscle hexokinase. They found that previous difficulties in getting an active hexokinase preparation from muscle was due to the acid reaction of water extracts, pH about 6.2. At this pH rapid inactivation of hexokinase occurred, but in investigating this phenomenon they found that enzyme activity could be restored by addition of dihydrocozymase. When the extracts were aged at pH 6 and dialyzed, the necessity for yet another co-factor was discovered, namely guanine. In such extracts either component alone was without effect, but when both guanine and dihydrocozymase were added hexokinase activity was restored.

#### EFFECT OF PITUITARY AND ADRENAL CORTEX EXTRACTS AND INSULIN OF THE HEXOKINASE REACTION<sup>2</sup>

Referring again to the simplified scheme of carbohydrate metabolism in figure 1, it may be seen that hexokinase initiates the utilization of glucose in the tissues and that if the activity of this enzyme were enhanced by

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<sup>2</sup> The experimental work reported in this section was carried out by S. P. Colowick, G. T. Cori, W. H. Price and M. W. Slein to whom should go the credit for these observations (10, 11).



insulin, most of the known effects of insulin in the intact animal could be explained. In spite of many trials an accelerating effect of insulin on the hexokinase reaction could not be demonstrated.

It then seemed possible that the clue to the situation might be in the reverse argument, namely, that if hexokinase were inhibited in the intact animal, hyperglycemia and glycosuria would result. With this in mind, experiments were carried out with muscle hexokinase preparations from rats made diabetic with alloxan. It was observed that in some cases the manometric measurements indicated a lag period of about 10 minutes duration before hexokinase activity set in and that addition of insulin abolished the lag period. Such an experiment is reproduced in figure 3.

Remembering the experiments of Houssay which demonstrated an amelioration of diabetes following the removal of the pituitary, we made the guess that the lag period may be due to an inhibitory pituitary factor present in the tissue extracts of alloxan diabetic rats. If this were so, the effect of insulin would consist in the removal of this inhibition. That a pituitary

Effect of Insulin on Hexokinase Activity of Diabetic Rat Muscle Extract.

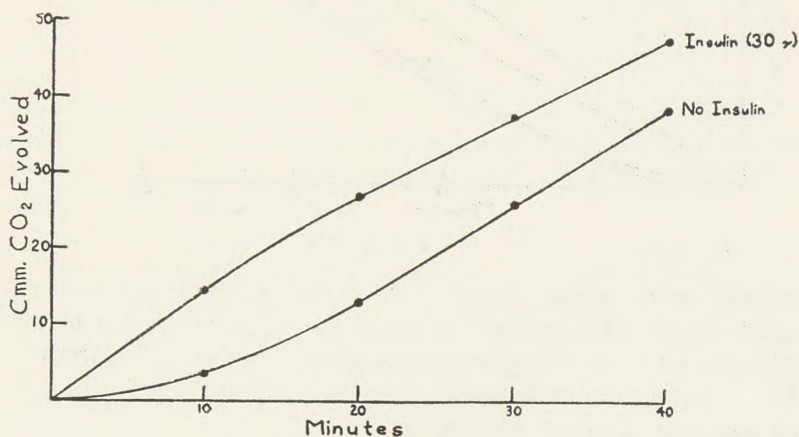


FIG. 3.

factor could cause the inhibition was suggested by the observation that curves for hexokinase activity similar to those shown in figure 3 were obtained in muscle extracts of normal rats previously injected with pituitary or in muscle extracts to which an isoelectric protein fraction of the pituitary was added in vitro (figure 4). Here again insulin counteracted the pituitary inhibition.

The short duration of the inhibition in figures 3 and 4 was attributed to the rapid destruction or inactivation of the pituitary factor in crude tissue



extracts. In order to eliminate some of the destructive factors, the hexokinase in muscle extract was purified by fractionation with acetone. A much more prolonged inhibition could be produced by addition of pituitary to such purified extracts (figure 5). Similar results were obtained when hexokinase prepared from an acetone powder of calf brain was used as the test system.

In view of the experiments reported by Long on the amelioration of diabetes after removal of the adrenals, it was of interest to study the effect

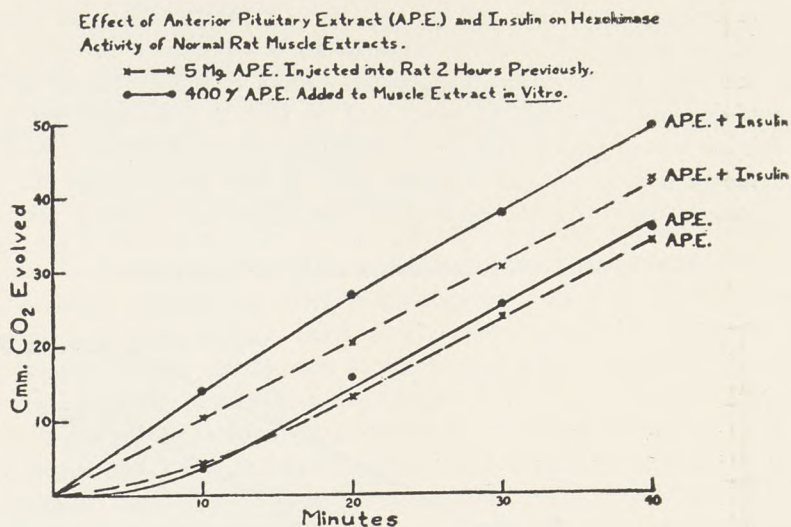


FIG. 4.

of adrenal cortex extract. Figure 5 shows that a commercial extract (Upjohn), by itself without effect, increased the inhibitory action of anterior pituitary on a purified hexokinase preparation. This effect of adrenal cortex extract is also seen in crude muscle extracts in which the action of pituitary alone is of short duration (figure 6).

The effect of adrenal cortex preparations has been made use of in an analysis of the hexokinase activity in crude muscle extracts of alloxan diabetic rats. It may be assumed that tissue extracts of normal animals contain insulin, and hence the hexokinase is free to act even if some pituitary factor is present; only if an excess of pituitary is added can an inhibition be demonstrated. In extracts of diabetic rats there should be a preponderance of the pituitary factor over insulin, because of the destruction of the islet tissue by alloxan. It would follow that if the extracts of diabetic rats contain the pituitary factor and no insulin, addition of adrenal cortex extract alone should produce inhibition. This is shown in figure 7. With-



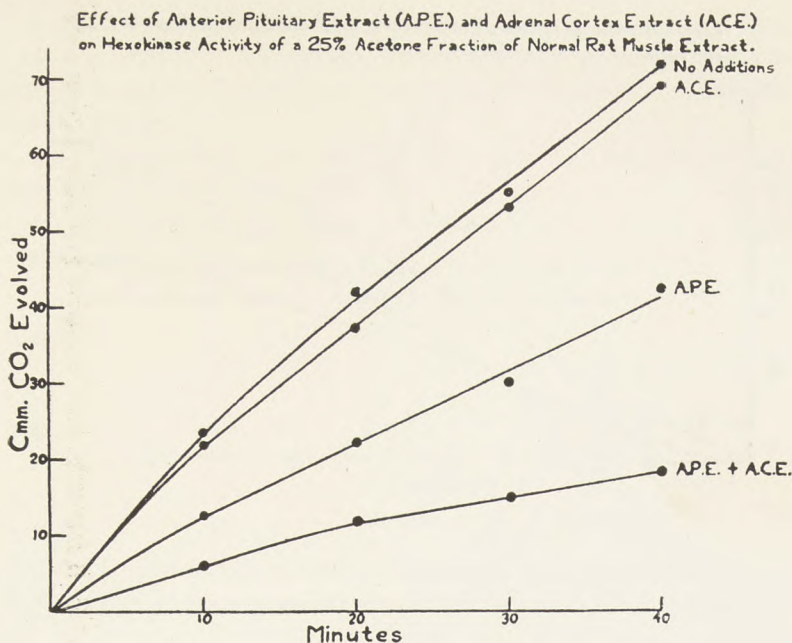


FIG. 5.

out addition of adrenal cortex extract there is a short lag period, with cortex extract added a marked inhibition occurs which in this case amounts to about 70 per cent for the 30-minute period, when compared with the sample to which insulin was added.

It should be emphasized that among 34 diabetic extracts investigated only 50 per cent showed a strong inhibition on addition of adrenal cortex extract alone and some gave completely negative results. This is probably due to several factors. Not all rats injected with alloxan get equally diabetic. If some islet tissue remained intact, the tissue extracts would contain insulin. Similarly, the lack of effect of adrenal cortex preparations alone on extracts from normal rats may be due either to less pituitary factor being present, or what seems more likely, to the presence of enough insulin to overcome the inhibition. Another factor is the instability of the inhibitory substance. When extracts from diabetic rats were kept for 1 to 2 hours at 0°, addition of cortex extract no longer produced inhibition, although the same extracts had given a positive result when tested immediately after preparation.<sup>3</sup> Finally, the optimal conditions for the extraction

<sup>3</sup> This recalls the interesting observations of Shorr (12), who found that muscle strips prepared from depancreatized animals showed initially an inhibition of glucose oxidation but that this inhibition disappeared when the tissues were kept for some hours in vitro under aerobic conditions.



Effect of Anterior Pituitary Extract (A.P.E.), Adrenal Cortex Extract (A.C.E.),  
and Insulin on Normal Rat Muscle Extract.

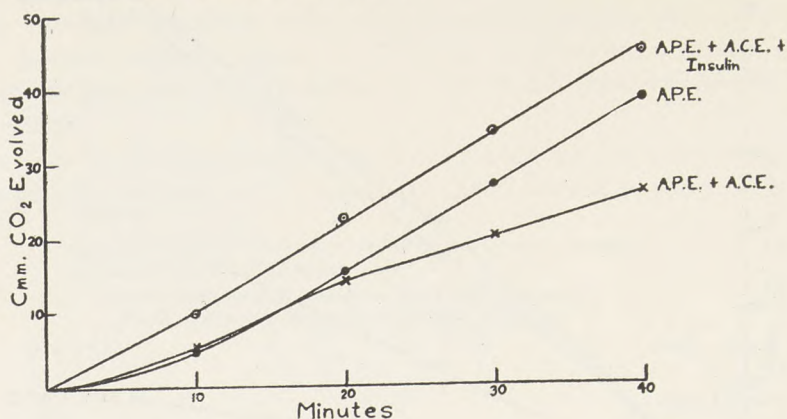


FIG. 6.

of the inhibitor from the tissues have not been worked out. The difficulty here is that both the inhibitor and the hexokinase must be extracted at the same time.

Further experiments with muscle extracts from diabetic rats are shown in figure 8. Addition of 10 micrograms of insulin had a suboptimal effect, while 50 micrograms completely released the inhibition caused by 0.1 cc. of adrenal cortex extract added to 2.5 cc. of reaction mixture. Next it was determined that addition of 0.05 cc. of cortex extract had as much inhibitory effect as 0.1 cc., while 0.01 cc. was suboptimal. The inhibitory action of the Upjohn extract could be reproduced with an amorphous fraction of the adrenal cortex, kindly supplied to us by Dr. Kendall and Dr. Kuizenga, but not with the crystalline compounds A, B and E of Kendall. The nature of the adrenal substance which causes this inhibition has not been determined.

The instability of the pituitary factor has so far prevented progress in its purification. Pituitaries from various species (beef, sheep, pig, horse) have yielded active extracts. It is essential that the glands be obtained as soon as possible after the death of the animals and that they be frozen immediately. The glands may be extracted for 30 minutes with dilute barium hydroxide, pH 10, followed by removal of barium with dilute sulfuric acid and separation of the isoelectric precipitate formed between pH 6.3 and 5.8. This precipitate, containing about 10 to 15 per cent of the extracted proteins, does not show any hexokinase activity of its own and inhibits brain hexokinase in the presence of adrenal cortex extract. The glands may also be extracted with dilute sulfuric acid at pH 5.7, followed by adjust-



ment to pH 5.3 and dilution. The precipitate formed on dilution contains most of the activity. Absorption on aluminum hydroxide has effected further purification. Lyophilized glands have occasionally yielded active material.

All the preparations so far obtained are unstable in solution and generally lose their activity when kept for 1 to 2 hours in an ice-bath. They could not be lyophilized or frozen in solution without loss of activity. It

**Effect of Adrenal Cortex Extract (A.C.E.) and Insulin  
on Hexokinase Activity of Diabetic Rat Muscle Extract.**

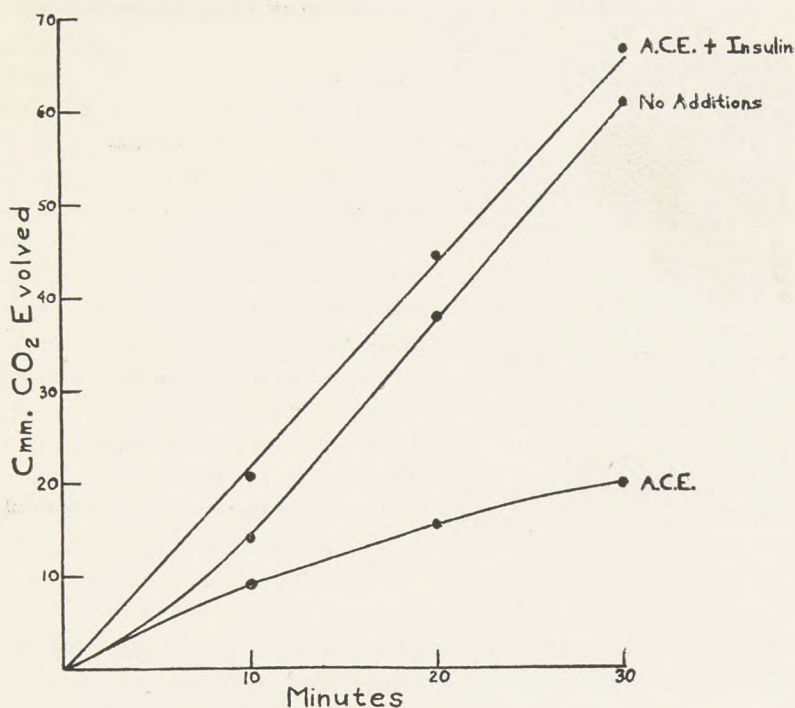


FIG. 7.

has not been possible so far to determine the nature of the destructive factors. Acetone fractionation could not be used because it caused inactivation of the pituitary factor.

A method of preparation which is successful in the majority of cases will be reported in detail. At the present stage of purification it did not seem profitable to try to identify the pituitary inhibitor of hexokinase with other factors known to be present in anterior pituitary extracts. A number of these factors have been tested on the hexokinase system with negative results. This would rule out unspecific inhibitory effects, as would the effect



of insulin in counteracting an existing inhibition. It may be mentioned here that this insulin effect is perfectly reproducible and that when insulin is reduced by cysteine or inactivated by treatment with alkali, it is no longer capable of counteracting the pituitary inhibition. Assuming that one is dealing with an interaction of proteins, a final analysis of the system would require that all three proteins, the enzyme, the inhibitor and the releasing agent, be available in relatively pure form.

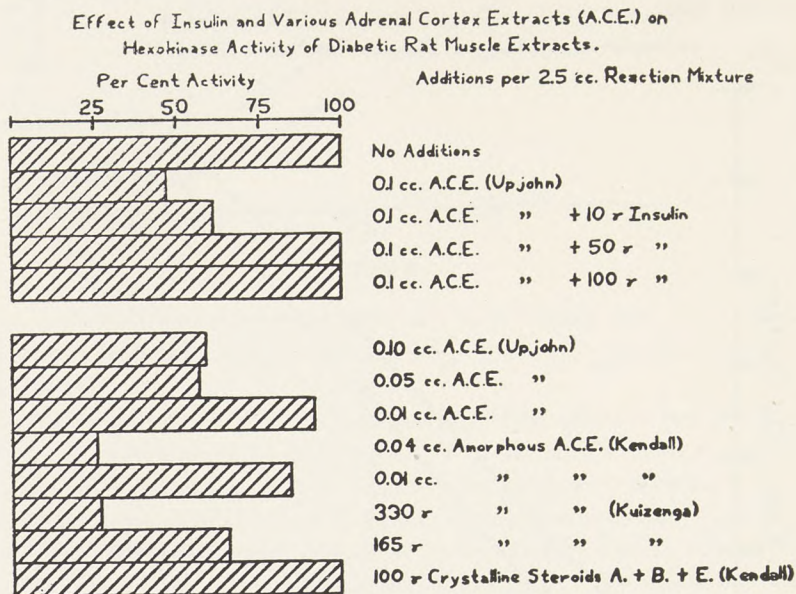


FIG. 8.

## DISCUSSION

The over-all reaction, glycogen  $\rightleftharpoons$  lactic acid, is not inhibited by the anterior pituitary fractions which inhibit the hexokinase reaction. There is also no inhibition of the reaction, glucose-6-phosphate  $\rightarrow$  glucose + phosphate, which occurs in the liver. Reference to figure 1 will show that the hexokinase reaction is not involved in either case. This would explain why lactate, pyruvate, alanine and other amino acids are convertible to glucose in the liver of depancreatized dogs and why injection of epinephrine in such dogs causes an excretion of extra sugar in the urine. In the latter case blood lactic acid derived from muscle glycogen would be converted to glucose in the liver.

Lukens (13) investigated the resynthesis of glycogen in previously stimulated muscles of normal and depancreatized cats. The amount of glycogen lost on stimulation was essentially the same in both types of animals and



the initial resynthesis of glycogen, presumably from hexosemonophosphate and lactate (which accumulate in muscle during stimulation) occurred at the same rate. However, the final restitution of the glycogen level which depends on the uptake of blood sugar by the muscles was delayed considerably in the depancreatized animals. The results of Lukens could therefore be explained by an inhibition of the hexokinase reaction in the diabetic animals.

Another observation which fits into this scheme is that of Bueding and coworkers (14). They showed that the rise in blood pyruvate which is seen in normal animals following the injection of glucose is absent in depancreatized dogs and that injection of insulin is necessary to bring back the increase in blood pyruvate in diabetic dogs. The normal animal responds with an increase in blood pyruvate, because the reactions leading to its formation occur somewhat faster than the reactions causing a removal of pyruvate. The removal of injected pyruvate from the blood occurs at the same rate in normal and diabetic dogs. It is also known that the muscles of diabetic dogs can convert their glycogen to pyruvate and lactate as rapidly as those of normal animals. As shown in figure 1, the lack of response of blood pyruvate to glucose injection could therefore be due to an inhibition of the hexokinase reaction and the effect of insulin to a release of this inhibition.

The idea that removal or destruction of the islet tissue of the pancreas results in under-utilization of blood sugar has recently received strong support in the experiments of Stetten and Klein (1) with deuterium. They found that in alloxan diabetic rats about 75 per cent of the urinary glucose was of dietary origin and that only 25 per cent represented gluconeogenesis. That certain amino acids, because they are convertible to glucose, are the source of gluconeogenesis, has long been accepted, and since there is an increased nitrogen excretion in the urine of depancreatized dogs, such animals convert more protein to sugar than do normal animals. In this sense there exists an overproduction of sugar in the diabetic animal, but this is of minor importance in comparison to the primary disturbance in carbohydrate metabolism which is in the utilization of blood sugar. Houssay's and Long's experiments have shown that this impairment of blood sugar utilization is due to a preponderance of anterior pituitary and adrenal cortex hormones over insulin. The present experiments would explain these phenomena by the action of anterior pituitary, adrenal cortex and insulin on hexokinase, an enzyme directly concerned with blood sugar utilization.

One more point deserves discussion here. The scheme in figure 1 indicates that a  $C_2$  intermediate is formed from both carbohydrate and fat which is then oxidized over a common pathway, a fact which is in itself of great



importance. Such oxidation cannot result in a gain of carbohydrate. A net gain would result, however, if a  $C_2$  fragment derived from fatty acids could be converted to pyruvate (by reductive carboxylation) or if two such fragments could condense to form a dicarboxylic acid, since the latter, as shown in the scheme, is convertible to carbohydrate. So far these reactions have not been observed in the animal body. The isotope studies with tracer carbon show interconversions between all three foodstuffs, carbohydrate, fat and protein, because the carbon fragments pass through a common metabolic pool, but they have given no indication that fatty acids are a source of gluconeogenesis (15).

A good deal of additional work will be required before a complete integration between experiments on the whole animal and on isolated enzyme systems can be achieved. It is possible that other points of action of anterior pituitary and insulin exist. The oxidation of glucose can be inhibited in the intact animal by the injection of a pituitary factor prepared by Greaves (16), and the oxidation can be accelerated by insulin *in vitro*, as shown in the experiment in figure 2. Finally, insulin may also have a direct stimulatory effect on some enzymatic reaction, as indicated by the fact that it produces hypoglycemia in hypophysectomized, adrenalectomized animals.

These possibilities are mentioned here in order to indicate the point of view that the writer has adopted, namely, that so far only a beginning has been made in the understanding of the mechanism of action by which hormones regulate the rate of enzymatic reactions in the body.

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## New Officers Announced at Alumni Banquet

More than 125 persons attended the annual Medical Alumni Association Banquet, held at 7 p. m., May 23, in Hotel Jefferson, St. Louis. Dr. Frank Ewerhardt, Dr. Robert A. Moore, and Dr. J. William Thompson were the speakers.

New officers of the Medical Alumni Association were announced as follows: President, Dr. Rogers Deakin; first vice-president, Dr. Theodore Hanser; second vice-president, Dr. Sim F. Beam; and secretary-treasurer, Dr. George Ittner.

Members of the executive committee are:

Terms expiring in 1948—Dr. Robert Mueller, Dr. Leo Gottlieb, Dr. Dudley Smith, and Dr. P. D. Stahl; terms expiring in 1949—Dr. A. Norman Arneson, Dr. Richard Paddock, Dr. David Skilling, and Dr. George Wulff; terms expiring in 1950—Dr. J. William Thompson, Dr. Louis H. Jorstad, Dr. Oliver Abel, Jr., and Dr. Samuel B. Grant.

The banquet was given in honor of the graduating seniors, who were welcomed by Dr. Thompson, outgoing president of the Association. He expressed the hope that a "huge reunion" would be held in 1948.

Dr. Robert A. Moore, Dean, related the serious problem of admissions to medical schools for the year 1947-1948. He explained that before 1941 the normal number of applications for admission to the Washington University School was 800. Now there are 1900 applicants for the 86 places in the freshman class. "And the rush is just beginning," he added.

Three new developments in the Medical School were revealed by Dr. Moore. First, a grant from the National Foundation for Infantile Paralysis for use by the Division of Physical Medicine obtained through the efforts of Dr. Ewerhardt; second, the Child Guidance Clinic to be started under grants from the Children's Research Foundation and the Social Planning Council, both of St. Louis; third, a teaching program in the field of cancer, aided by a grant from the National Advisory Cancer Council.

Dr. Moore closed his talk by saying, "If we are not already one of the best medical schools, we'll make ourselves that soon and stay there for the rest of time."

Dr. Frank Ewerhardt traced the development of physical therapy to its present recognition as a specialty. Its practice became generally known following successful application during the first world war, and developed to greater importance in the recent world conflict. Dr. Ewerhardt, who



organized a department of physical therapy here in 1915, emphasized the importance to the individual of having outside interests as well as a satisfying vocation.

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### **Graduate Course for Technicians**

A course in recent advances in clinical pathology will be offered for laboratory technicians by the Division of Postgraduate Studies on Nov. 17 and 18, 1947.

Designed as a period of postgraduate training, this review should be of particular benefit to technicians whose duties have not permitted an opportunity for keeping abreast of newer developments. The material will be applicable to some or all phases of work for technicians employed in hospitals, industry, clinics, or physician's offices.

The course will consist of lecture, discussion, and demonstration periods in two sessions on each of the two days.

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## **Diagnostic Unit Opened at Mallinckrodt on May 1**

The Mallinckrodt Institute of Radiology officially opened a newly-equipped diagnostic unit on the ground floor of the building on May 1. This is probably the newest and most modern department of its kind in the country, and includes the latest developments in diagnostic equipment.

There are five diagnostic rooms, each equipped for taking special types of X-rays such as chest, skull, sinus, stereoscopic films of the mastoids, spine, and routine miscellaneous films.

The purpose of the diagnostic unit is to increase the capacity of the Department, and to render efficient and prompt service to ambulatory patients, whether in or out of the hospital. Its location will be convenient for examining patients referred from Washington University Clinics, Barnes Doctors' Offices, Children's Hospital, and private patients referred from the outside.

Hospital patients who are confined to beds, wheel chairs, or stretchers, as well as those requiring more difficult diagnostic procedures, will continue to be examined on the second floor.

A photo-fluorographic unit, to be used in making chest surveys on large groups of patients, has been installed on the ground floor. This equipment uses 70 mm. roll film with an automatic timer to produce uniform exposures.



The large films are developed, hypoed, washed, and dried by the new Pako Automatic Film Processing Machine. This unit is the first of its type to be installed in any hospital in this country. Only 47 minutes are required from the time the film is exposed until it is ready for labeling.

To further shorten the film handling time, an electric conveyer was designed by Mr. Boling, of the Barnes Hospital Maintenance Department, to transport the films from the ground floor to the first floor. This ingenious conveyer answers a problem which manufacturers could not solve.

The opening of this new unit more than doubles the capacity for taking diagnostic X-ray films. It represents the expenditure of many thousands of dollars, and was developed to give better service to both patients and doctors.

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## Dr. Carl Cori Receives Prize for Metabolism Work

For distinguished achievements in the field of human metabolism extending over a period of 20 years, Dr. Carl F. Cori, professor of biological chemistry and pharmacology, was awarded the second intermediate Sugar Research Prize of \$5,000. The award was made at the Sugar Research Foundation's annual dinner at the Yale Club in New York City on April 28.

The award is given annually by the National Science Fund of the National Academy of Sciences in recognition of the development of original knowledge about sugar. In 1950 a grand prize of \$25,000 will be given for the most important discovery in terms of the advancement of knowledge or public benefit during the preceding five years.

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## Dr. Thomas Hunter Appointed Assistant Dean

The appointment of Dr. Thomas Hunter as assistant dean for students was announced by Dr. Robert A. Moore. Dr. Hunter comes to St. Louis from Columbus University College of Physicians and Surgeons, where he has been instructor in medicine.

Upon graduation from Harvard College, Dr. Hunter received the Henry Fellowship for study in England. He was at Cambridge University from



1935 to 1938 and returned to Harvard to take his medical degree in 1940. He was successively interne, assistant resident, and chief resident in medicine at the Presbyterian Hospital in New York. He has been active in the study of the treatment of subacute bacterial endocarditis with penicillin.

At Washington University, Dr. Hunter will be an assistant professor of medicine and assistant dean in charge of students. As assistant dean, he will participate in the activities of the Admissions Committee, advise students during their four years of undergraduate medicine, and assist both students and graduates in securing internships and residencies.

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### **Division of Gerontology Established**

The establishment of a separate division of gerontology was authorized by the executive faculty of the School of Medicine on July 1, 1947. The new division will be administered directly by the Dean's Office, with Dr. William Kountz and Dr. Esben Kirk, newly-appointed assistant professor of medicine, in charge.

It was through the efforts of Dr. Kountz that a special fund was established in the department of medicine several years ago for the study of aging. With the growth of this project, it is desirable now to give it recognition as a separate division.

Dr. Kirk secured his medical training in Copenhagen, Denmark, where he was born. From 1931 to 1934 he was an assistant resident physician at the Hospital of the Rockefeller Institute for Medical Research in New York, where he studied under Dr. D. D. Van Slyke.

Laboratories for the new division of gerontology will be housed at the Isolation Hospital of the City of St. Louis.

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## **New Grants Awarded to Medical School**

Three significant grants to the School of Medicine were announced recently by Dr. Robert A. Moore, Dean. They are from the National Foundation for Infantile Paralysis, the National Advisory Cancer Council, and the Children's Research Foundation of St. Louis.

A grant for the establishment of a division of physical medicine on a full-time basis has been awarded by the National Foundation for Infantile Paralysis. Dr. Moore stated "the long labors of Dr. Ewerhardt will, with this grant, be rewarded." It will be possible to correlate the activities of the school of physical therapy, the department of occupational therapy, and the service functions of physical medicine in the hospital. Recognition of



this division also will represent a future step in our teaching program.

The National Advisory Cancer Council has voted sufficient funds for the School of Medicine to add to the staff one person who will be concerned primarily with teaching and service in the field of cancer. This person will be appointed in some department and, with the cooperation of all departments, will administer the tumor clinic. A grant from the Missouri Chapter of the Cancer Society will provide the non-professional assistance needed to effectuate this program.

A generous grant to establish a child guidance clinic comes to the School from the Children's Research Foundation of St. Louis. Dr. Moore said that this will be a joint activity in the departments of neuropsychiatry and pediatrics in the School of Medicine, the George Warren Brown School of Social Work, and the departments of education and psychology of the College. The clinic will be located in the house adjacent to the north building of the Medical School.

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### **Medical School Admits Negroes**

Chancellor Arthur H. Compton announced on July 3 that the Board of Directors of Washington University had approved admission of Negroes to the School of Medicine.

"In view of the recent increase in the number and scope of postgraduate courses in the School of Medicine," he stated, "the board is of the opinion that Washington University is in a position to render an unusual service to the education of Negro physicians and surgeons of this country."

Prior to the announcement, Dr. James W. Nofles of St. Louis was enrolled in June, and completed a three-week postgraduate course in ophthalmology under the new ruling. He is a graduate of Howard University, Washington, D. C.

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### **Dr. Oliver Lowry Heads Pharmacology Department**

Chancellor Arthur Compton announced recently that Dr. Oliver Lowry has accepted the appointment as professor of pharmacology and head of the department. The appointment was effective July 1, 1947.

Dr. Lowry took his undergraduate work at Northwestern University, graduating in 1932. Subsequently, he studied at the University of Chicago and Rush Medical College, where he received his Ph.D. and M.D. degrees respectively. After five years as a member of the department of biological chemistry at Harvard Medical College, he joined the staff of the Public Health Research Institute of New York City in 1942 and has been there for the past five years.



Most recent of Dr. Lowry's contributions to medical science is the development of microchemical methods for the determination of vitamins and other substances in the blood.

Dr. Lowry will arrive in St. Louis about December 1, 1947.

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### **Radiation Course Given in May**

A course in the physics of radiation and the treatment of gynecological cancer was given during May at the Mallinckrodt Institute of Radiology.

Dr. James F. Nolan, Dr. G. F. Fraser, Dr. Martin Kamen, and Dr. A. Norman Arneson handled instruction of the fifteen people who took the course.

Attending from outside the state were Dr. John A. Wall, gynecologist from the M. D. Anderson Hospital for Cancer Research at the University of Texas; Dr. Tu-shan Jung, fellow of the American Bureau of Medical Aid to China; and Dr. Michelle Berger of the Radium Institute of Paris.

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### **Class of '42 Holds Reunion by Mail**

Charles B. Mueller, M.D., of the class of '42 recently completed a news letter for the fifth anniversary of that class, and sent it to all the members, whom he could contact. Called "The Forty-Two Review," it gives a brief resume of activities and personal notes for 72 out of 93 in the class. Dr. Mueller wrote letters to all those for whom he could find addresses and received fine responses from 60 per cent. The Alumni Office furnished its address list, and will be glad to help other class members in similar efforts.

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### **Opportunity for Physician in Alma, Mo.**

A note from Dr. John G. W. Fischer, '98, in Alma, Mo., reads as follows:

"I just came back from a two weeks' stay in the hospital, and I am yearning to retire if I can succeed in inducing a physician to come here. If you know of a doctor who wishes to make a change, send him here, for I have a fine set-up for one. I am close to 76 years old and have been here 49 years."

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### **Dr. Gerty Cori Promoted to Professor**

Dr. Gerty T. Cori, associate professor of research biological chemistry, has been promoted to professor of biological chemistry, effective July 1, 1947.

Dr. Cori, who is the wife of Dr. Carl Cori, has made many notable contributions to biological chemistry. She is currently working on enzymes and carbohydrate metabolism.



Dr. Cori's most recent paper is "The Effect of Adrenal Cortex and Anterior Pituitary Extracts and Insulin on the Hexokinase Reaction," written with the aid of two other members of the department. She has been with Washington University since 1931, and received her M.D. from the University of Prague in 1920.

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## Faculty Changes and Appointments

Eighty-nine new appointments and promotions were approved at the last meeting of the Executive Faculty. Dr. Thomas Hunter was appointed assistant dean in charge of students and assistant professor of medicine. Dr. Robert I. Watson was appointed assistant dean and associate professor of medical psychology.

### **Anatomy**

Dr. Oliver Duggins, appointed research assistant.

### **Bacteriology and Immunology**

Miss Frances Kimura, appointed instructor.

### **Biological Chemistry**

Dr. J. Oliver Lampen, appointed instructor; Dr. Gerty T. Cori promoted to professor.

### **Internal Medicine**

Dr. Esben Kirk, appointed assistant professor of medicine and director of research in the Division of Gerontology; Dr. Axel Gronau, appointed assistant in clinical medicine; Dr. Samuel Bukantz, appointed instructor in medicine; Dr. Arnold H. Williams, appointed research assistant in medicine; Dr. Grace Bergner, appointed assistant in clinical medicine.

Appointed instructors in clinical medicine: Dr. David Kerr, Dr. William G. Becke, Dr. Walter Baumgarten, Dr. Melvin Kirstein, and Dr. Loren F. Blaney. Appointed assistants in medicine: Dr. David Graham, Dr. William Daughaday, Dr. Gladden V. Elliott, Dr. Ernest T. Rouse, Dr. James Kirsch, Dr. Carl L. Cook, Dr. William M. Daily, Dr. James F. Tagge, Dr. Laurence K. MacDaniels, Dr. James Owen, and Dr. H. Mitchell Perry.

Dr. Charles Shaffer, appointed assistant in medicine in residence at Los Alamos.

### **Dermatology**

Dr. James W. Bagby appointed instructor in clinical dermatology.



### **Neuropsychiatry**

Appointed assistants in neuropsychiatry: Dr. Gregory C. Gressel, Dr. Donald Meltzer, Dr. Arnold Scheibel, Dr. Edward Kowert, Dr. Jackson C. Neavles, Dr. Marshall D. Schechter, Dr. Philip H. Starr.

Dr. Frances K. Graham, appointed part-time instructor in medical psychology; Mrs. Betty McDonald Caldwell, appointed assistant in medical psychology.

### **Obstetrics and Gynecology**

Dr. William H. Masters, appointed instructor in obstetrics and gynecology; Dr. Edgar H. Keys, Jr., Dr. Claud C. Young, Dr. James Pennoyer, and Dr. Trowbridge R. Mafit, appointed assistants in obstetrics and gynecology.

### **Ophthalmology**

Dr. Theodore E. Sanders and Dr. Adolph C. Lange, promoted to assistant professors of clinical ophthalmology; Dr. John Helm, appointed assistant in ophthalmology.

### **Otolaryngology**

Dr. Edward H. Lyman and Dr. James L. McCrory, appointed instructors in clinical otolaryngology; Dr. G. O'Neil Proud, title changed to instructor in clinical otolaryngology.

### **Pathology**

Dr. Betty Ben Geren and Dr. John B. Frerichs, appointed instructors in pathology; Dr. Vol K. Phillips and Dr. Joyce S. Davis, appointed assistants in pathology; Robert L. Hunter and Mrs. Eleanor Lerner Wenger, appointed research assistants in pathology.

### **Pediatrics**

Dr. Gilbert Forbes and Dr. Merl J. Carson, promoted to assistant professors of pediatrics; Dr. James Goodfriend and Dr. Donald Thurston, appointed instructors in pediatrics; Dr. Wayne A. Rupe and Dr. Edwin H. Rohlfing, appointed instructors in clinical pediatrics. Appointed assistants in pediatrics: Dr. William Davis, Dr. Gene Grabau, Dr. James Kinder, Dr. Walter Kennedy, Dr. William G. Klingberg, and Dr. Bailey Webb.

### **Pharmacology**

Dr. Oliver Lowry, appointed professor of pharmacology.

### **Physiology**

Dr. Albert Roos, appointed instructor in physiology; Miss Doris Rolf, appointed research assistant in physiology.



### **Radiology**

Dr. Mildred Trotter, appointed consultant in anatomy to the department of radiology. Appointed assistants in radiology: Dr. Joseph Norton, Dr. G. G. Zedler, Dr. James Little, Dr. E. G. Anderson, and Dr. James Steele.

### **Surgery**

Dr. Robert Elman, Dr. Peter Heinbecker, and Dr. Nathan Womack, promoted to professors of clinical surgery; Dr. Maurice B. Roche, appointed instructor in clinical orthopedic surgery; Dr. F. Louis Knotts, appointed instructor in surgery; Dr. William F. Rose, appointed instructor in clinical surgery; Dr. Sam Schneider, appointed assistant in clinical surgery; Dr. Eugene M. Bricker, title changed to associate professor of clinical surgery.

Appointed assistants in surgery; Dr. Richard T. Odell, Dr. David R. Oliver, Dr. C. Barber Mueller, and Dr. John F. Neville, Jr.

### **Resignations**

Dr. John H. Van Dyke, assistant professor of anatomy, effective June 30, 1947; Dr. Russell Blattner, associate professor of pediatrics, Dr. Florence Heys, instructor in biology in pediatrics, and Mrs. Anne E. Royer, instructor in medical psychology, all effective Aug. 31, 1947.

### **Miscellaneous**

Miss Bettye Jo Case replaces Mrs. Joyce Greaves, who resigned in June, as administrative secretary to the dean. She is a graduate of the School of Journalism at the University of Missouri and will handle all news releases for the School of Medicine.

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## **Departmental News**

### **Surgery**

Dr. Evarts A. Graham, professor of surgery, gave the centennial address at the American Medical Association meeting in Atlantic City, N. J., June 9-14.

Dr. Oscar P. Hampton, instructor in clinical orthopedic surgery, spoke at Fitzsimmons General Hospital in Denver on May 6. His topic was, "Civilian Application of Advances in the Management of Compound Fractures and Joint Injuries During World War II."

Dr. Robert Elman, professor of clinical surgery, attended a meeting of the Professional Advisory Committee of the Vocational Rehabilitation Service in Washington, D. C., May 12 and 13. On May 23, he was present at a meeting of the Surgery Study Section of the National Institute of Health.



A certificate of Merit and Gold Medal for Scientific Accomplishments were presented to Dr. Vilray P. Blair on May 20 by the St. Louis Medical Society for his pioneer work in plastic surgery.

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### **Radiology**

Dr. Sherwood Moore, professor of radiology, attended the meeting of the American Cancer Society in New York City on June 5. He is Director-at-Large of the Society.

Dr. Wendell G. Scott, associate professor of clinical radiology, was guest speaker at the annual meeting of the Indiana Roentgen Society in Indianapolis on May 18. His subject was "Prolapse of the Gastric Mucosa into the Duodenum as a Cause of Gastro-Intestinal Symptoms."

Dr. William Stanbro, resident in radiology, will be professor of radiology at George Washington University next fall.

Dr. A. Norman Arneson was installed as president of the American Radium Society in Atlantic City, June 9.

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### **Pediatrics**

Dr. Russell J. Blattner, associate professor of pediatrics, will leave next fall to become professor of pediatrics at Baylor University Medical School in Houston, Tex. He gave a paper on "Epidemiology of St. Louis Encephalitis," of which he is a co-author, at the American Pediatric Society meeting in Stockbridge, Mass., May 13-15.

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### **Anatomy**

Dr. E. V. Cowdry, professor of anatomy, delivered the convocation address at the installment of George D. Stoddard as president of the University of Illinois, held at the medical school in Chicago on May 15.

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### **Medicine**

Dr. W. Barry Wood, Jr., and Miss Mary Smith presented a paper entitled "Phagocytoses of Virulent Encapsulated Bacteria in the Absence of Antibody" at a meeting of the Society of American Bacteriologists in Philadelphia May 13.

Sixteen members of the Department attended the Association of American Physicians meeting at Atlantic City, N. J., in May.



## Publications by the Staff of the School of Medicine

### April - June, 1947

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## Alumni News

1893

**J. J. Meredith** has moved from St. Louis to Cleveland, Ohio.

**John Massie**, now practicing in Belleville, Ill., also asks about a class reunion. "Still going along the path life and duty require, to this organic path of existence. I hope to finish my first fifty years, if not the second," he writes.

"No more maternity cases the past year," reports **Drura Claiborn** of Big Timber, Mont. He says he is still fairly active, but slowing up some.

**George Orrick** is at Western Oklahoma Hospital in Fort Supply, Okla., where he has been for seven years. He says, "I'm in very good health and working hard as assistant physician."

1903

**G. W. Walker** died Nov. 13, 1946, in Cape Girardeau, Mo.

1907

**G. D. Royston** spoke on The Diagnosis and Treatment of Uterine Bleeding at the annual meeting of the Missouri Pacific Railroad Association in St. Louis, March 20. He also addressed the Iowa State Medical Society in Des Moines on the same subject during April.

1912

**Harry A. Brandes** of Bismarck, N. Dak., passed away on May 12, 1947.

1925

**L. E. Ellison** has moved from Warren, Ark., to Maplewood, Mo.

1927

**Eleanora Schmidt** has moved from Norman, Okla. to De Soto, Mo.

1932

**Edwin Chunghoon** is in Honolulu, Hawaii.

1933

**R. M. Van Matre** was discharged from the army as a lieutenant-colonel and has taken up practice in Topeka, Kan.

**Lyman Richardson** has moved from Kansas City to the Veterans' Administration Hospital in New Orleans.

1934

**E. R. Bohrer** dropped into the Alumni Office to report his change in address from West Plains to Jefferson City, Mo. After five years in the army, he was a major when discharged.

**Everett Caldemeyer** is practicing in Evansville following his discharge from the army.

**Paul Kunkel** has changed his title from Captain back to Doctor, and is at the Veterans' Administration Hospital, Newington, Conn.

1935

**Lester Allison** has moved to Springfield, Ill. He was formerly in East St. Louis.

**Mary C. Abney** of Richland, Wash., died May 20, 1947.

1937

**Joseph Pontier** has moved from Frisco, Calif., to Richmond, Calif.

1938

**Theodore Lynn** is practicing orthopedic surgery in Los Angeles.

**Kenneth L. Carter** is in Beloit, Wis., at the Beloit Clinic.



1939

**G. A. Slusser** is now at Watts Clinic in Silver City, N. Mex.

1940

**Seymour Brown** was elected secretary of the newly-organized St. Louis Society of Anesthesiologists. He is director of anesthesiology, St. John's Hospital, and director of anesthesia at St. Louis County Hospital.

**Gordon Moore** writes that he has been in Alton, Ill., for almost a year, and confines his practice to surgery. He reports that there are a number of W. U. graduates in practice there, and all doing splendid jobs.

1941

**James Kinder, Jr.** has moved from Cape Girardeau, Mo. to Denver.

1942

**Charles Lockhart** is on the staff of Ellis Fischel State Cancer Hospital in Columbia, Mo.

1943

**Harold E. Walters** was discharged from the army in February and will be resident in surgery at St. Luke's, St. Louis, for the next year.

**John Wilson** wrote a long letter telling of his assignment to Fifth Army Headquarters General Dispensary in Chicago. After a year in the army, he says he is looking forward to the time when he can return to civilian medicine.

**James N. Haddock** is a fellow at Menninger Foundation School of Psychiatry, Topeka, Kans.

**Forrest C. Lawrence** is starting a general practice in Bartlesville, Okla.

**Jerry H. Allen, Jr.** reports that Jerry H. Allen, III was born Jan. 19,

1947 at Los Alamos, N. Mex. Mrs. Allen is the former Frances Fisher, B.S., R.N., Washington University, '45.

**Joseph Mallory** has moved from St. Louis to Arlington, Kans.

**William Welborn** is in the army, now stationed at Battle Creek, Mich.

1944

**Clayton H. Manry** is with the Department of Internal Medicine at the University of Syracuse.

**Klaus R. Dehlinger** writes that he has just started a three-year residency in radiology at Peter Bent Brinham Hospital, Boston. His wife, Jean, of the April '43 class, is a housewife at present, taking care of their two sons, aged two years and six months.

**John M. Arthur, III** is taking post-graduate training in psychiatry. He is a member of the staff of Spring Grove Hospital (for mental illness) in Catonsville, Md., where he has been since his discharge from the army in August, 1946.

**M. P. Meisenheimer** recently started a general practice in Prospect Heights, Ill.

1945

**Edmond Bechtold** has moved to Belleville, Ill., from West Palm Beach, Fla.

1946

**R. Robert Bates** writes that he has taken a surgical residency at St. Mary's Hospital, Tucson, Ariz.

**Stanley Thiel, Gladden Elliott, and James W. Owen, Jr.,** are at Barnes Hospital, St. Louis.

**Ann DeHuff**, now Mrs. R. M. Peters, is at Station Hospital in Ft. Myers, Va.



**F. A. Elders, Jr.**, is in Rolla, Mo.

**Stanley E. Roberts**, who is on the resident staff of St. Luke's in St. Louis, reports that he is married and has one daughter.

**Marvin Gibstine** and **Jack Wiedershine** both are at Jewish Hospital in St. Louis.

**Walter F. Scott, Jr.**, is a resident in pathology at Jefferson-Hillman Hospital in Birmingham, Ala.

**Theodore Smith** is in Temple, Tex., at Scott and White Clinic there.

**Gilbert Chamberlain** is on the staff of New York Hospital in New York City.

**Andrew Lanier** is a resident in surgery at the Marine Hospital in San Francisco.

(Editor's Note: Cards have been received from 21 members of the class of '46 who expected to be in some branch of the service after July 1, 1947.)



# WASHINGTON UNIVERSITY

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Arthur H. Compton, Ph.D., Sc.D., LL.D., *Bridge Chancellor*

Charles Belknap, B.S., *Vice Chancellor*

Joyce C. Stearns, Ph.D., LL.D., *Dean of Faculties*

Thomas Edward Blackwell, Ph.B., M.S., J.D.,  
*Director of Business Administration*

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The College of Liberal Arts

Stuart A. Queen, Ph.D., Dean

The School of Engineering

Alexander S. Langsdorf, M.M.E., Dean

The School of Architecture

Alexander S. Langsdorf, M.M.E., Dean

The School of Business and Public Administration

Isaac Lippincott, Ph.D., Acting Dean

The George Warren Brown School of Social Work

Benjamin E. Youngdahl, A.M., Dean

The Henry Shaw School of Botany

George T. Moore, Ph.D., Director

The School of Graduate Studies

Carl Tolman, Ph.D., Dean

The School of Law

Wayne L. Townsend, A.B., LL.B., J.S.D., Dean

The School of Medicine

Robert A. Moore, M.D., Ph.D., Dean

The School of Dentistry

Otto W. Brandhorst, D.D.S., Dean

The School of Nursing

Louise Knapp, R.N., B.S., A.M., Director

The School of Fine Arts

Kenneth E. Hudson, B.F.A., Dean

University College

Willis H. Reals, Ph.D., Dean

The Summer School

Frank L. Wright, A.M., Ed.D., Director

Mary Institute, a preparatory school for girls, located at Ladue and Warson Roads, is also conducted under the charter of the University.

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**Note:** Complete information about any of the schools listed above may be obtained by writing to the Dean or Director concerned.